

IN THE CLAIMS

Kindly cancel, without prejudice, claims 16, 17, 20, 23-42, 44, 46, 47, 49 and 50. Please add claims 51-72 as follows:

51. An HLA-DR typing process comprising the steps of:

(a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being selected from the group consisting of:

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- (i) the DNA sequence of DNA insert DR- β -A, DR- β -B or DR- β -C;
 - (ii) the expressed portion of the DNA sequence of DNA insert DR- β -A, DR- β -B or DR- β -C;
 - (iii) a DNA sequence that, upon expression, codes for a portion of a polypeptide encoded by any one of the foregoing DNA sequences, said portion comprising a region of mismatch between any two of the foregoing DNA sequences;
 - (iv) a DNA sequence that hybridizes to any one of the foregoing sequences; and
 - (v) a DNA sequence which differs from any one of the foregoing DNA sequences in codon sequence due to the degeneracy of the genetic code; and

(b) detecting areas of hybridization between said DNA in said sample and said DNA sequence.

52. An HLA-DR typing process comprising the steps of:

(a) restricting a first DNA isolated from an individual to be typed with at least one restriction endonuclease;

(b) size-fractionating said restricted DNA;

(c) hybridizing said size-fractionated DNA to be typed to a second DNA, said second DNA being selected from the group consisting of:

- D2
- (i) the DNA sequence of DNA insert DR- β -A, DR- β -B or DR- β -C;
 - (ii) the expressed portion of the DNA sequence of DNA insert DR- β -A, DR- β -B or DR- β -C;
 - (iii) a DNA sequence that, upon expression, codes for a portion of a polypeptide encoded by any one of the foregoing DNA sequences, said portion comprising a region of mismatch between any two of the foregoing DNA sequences;
 - (iv) a DNA sequence that hybridizes to any one of the foregoing sequences; and
 - (v) a DNA sequence which differs from any one of the foregoing DNA sequences in codon

sequence due to the degeneracy of the genetic code; and

(d) detecting areas of hybridization between said size-fractionated DNA and said second DNA.

53. An HLA-DR typing process comprising the steps of:

(a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being capable of hybridizing to a polymorphic region of an HLA-DR- β -chain locus to allow determination of one or more HLA alleles for use in HLA-DR- β typing, said polymorphic region being encoded by DNA selected from the group consisting of:

- P2
- (i) a DNA sequence encoding amino acids 8-14, 26-32 or 72-78 of said locus;
 - (ii) a DNA sequence which is fully complementary to any one of the DNA sequences of (i); and
 - (iii) a DNA sequence which differs from any one of the DNA sequences of (i) in codon sequence due to the degeneracy of the genetic code; and

(b) detecting areas of hybridization between said DNA in said sample and said DNA sequence.

54. An HLA-DR typing process comprising the steps of:

(a) restricting a first DNA isolated from an individual to be typed with at least one restriction endonuclease;

(b) size-fractionating said restricted DNA;

(c) hybridizing said size-fractionated DNA to be typed to a second DNA, said second DNA being capable of hybridizing to a polymorphic region of an HLA-DR- β -chain locus to allow determination of one or more HLA alleles for use in HLA DR- β typing, said polymorphic region being encoded by DNA selected from the group consisting of:

- P2
- (i) a DNA sequence encoding amino acids 8-14, 26-32 or 72-78 of said locus;
 - (ii) a DNA sequence which is fully complementary to any one of the DNA sequences of (i); and
 - (iii) a DNA sequence which differs from any one of the DNA sequences of (i) in codon sequence due to the degeneracy of the genetic code; and

(d) detecting areas of hybridization between said size-fractionated DNA and said second DNA.

55. An HLA-DR typing process comprising the steps of:

(a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being selected from the group consisting of:

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(i) GGGGACACCCGACCACGTTTCTTGAGCTGCTTAAGTCTGAGT
GTCATTTCTCAATGGGACGGAGCGGGTGCGGTTCTTGAGAGA
CACTTCCATAACCAGGAGGAGTACGCGCGCTTCGACAGCGACG
TGGGGGAGTACCGGGCGGTGAGGGAGCTGGGGCGGCCTGATGC
CGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCGG
GGCCAGGTGGACAATTACTGCAGACACAACCTACGGGGTTGTGG
AGAGCTTCACAGTGCAGCGGCGAGTCCATCCTCAGGTGACTGT
GTATCCTGCAAGACCCAGCCCCTGCAGCACCACAACCTCCTGG
TCTGCTCTGTGAGTGGTTTCTATCCAGGCAGCATTGAAGTCAG
TGGTTCCCGAACGGCCAGGAAGAGAAGGCTGGGGTGGTGTCCA
CGGGCCTGATCCAGAATGGAGACTGGACCTTCCAGACCCTGGT
GATGCTAGAAACATTTCTCCTCGGAGTGGAGAGGTTTACACCTGC
CAAGTGGAGCACCCAAGCGTAACGAGCCCTCTCACAGTGAAT
GGAGTGCACGGTCTGAATCTGCACAGAGCAAGATGCTGAGTGG
AGTCGGGGGCTTTGTGCTGGGCCTGCTCTTCCTTGGGGCCGGG
CTGTTTATCTAOTTCAGGAATCAGAAAGGACACTCTGGACTTC
AGCCAACAGGATTCCTGAGC;

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(ii) GGGGACACCCGACCACGTTTCTTGAGCAGGTTAAACATGAGT
GTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGACAG
ATACTTCTATACCAAGAGGAGTACGTGCGCTTCGACAGCGAC
GTGGGGGAGTACCGGGCGGTGACGGAGCTGGGGCGGCCTGATG
CCGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCG
GGCCGCGGTGGACACCTACTGCAGACACAACCTACGGGGTTGGT
GAGAGCTTCACAGTGCAGCGGCGAGTCTATCCTGAGGTGACTG
TGTATCCTGCAAAGACCCAGCCCCTGCAGCACCACAACCTCCT

GGTCTGCTCTGTGAATGGTTTCTATCCAGGCAGCATTGAAGTC
AGGTGGTTCCGGAACGGCCAGGAAGAGAAGACTGGGGTGGTGT
CCACAGGCCTGATCCAGAATGGAGACTGGACCTTCCAGACCCT
GGTGATGCTGGAAACAGTTCCTCGGAGTGGAGAGGTTTACACC
TCCCAAGTGGAGCACCCAAGCCTGACGAGCCCTCTCACAGTGG
AATGGAGAGCACGGTCTGAATCTGCACAGAGCAAGATGCTGAG
TGGAGTCGGGGGCTTCGTGCTGGGCCTGCTCTTCCTTGGGGCC
GGGCTGTTCATCTACTTCAGGAATCAGAAAGGACACTCTGGAC
TTCAGCCAACAGGATTCCTGAGC;

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(iii) a DNA sequence which is fully complementary
to the DNA sequence of (i) or (ii); and

(iv) a DNA sequence which differs from the DNA
sequence of (i) or (ii) in codon sequence
due to the degeneracy of the genetic code;
and

(b) detecting areas of hybridization between said
DNA in said sample and said DNA sequence.

56. An HLA-DR typing process comprising the steps
of:

(a) restricting a first DNA isolated from an
individual to be typed with at least one restriction
endonuclease;

(b) size-fractionating said restricted DNA;

(c) hybridizing said size-fractionated DNA to be typed to a second DNA, said second DNA being selected from the group consisting of:

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(i) GGGGACACCCGACCACGTTTCTTGGAGCTGCTTAAGTCTGAGT
GTCATTTCTCAATGGGACGGAGCGGGTGCGGTTCTTGAGAGA
CACTTCCATAACCAGGAGGAGTACGCGCGCTTCGACAGCGACG
TGGGGGAGTACCGGGCGGTGAGGGAGCTGGGGCGGCCTGATGC
CGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCGG
GGCCAGGTGGACAATTACTGCAGACACAACCTACGGGGTTGTGG
AGAGCTTCACAGTGCAGCGGCGAGTCCATCCTCAGGTGACTGT
GTATCCTGCAAGACCCAGCCCCTGCAGCACCACAACCTCCTGG
TCTGCTCTGTGAGTGGTTTCTATCCAGGCAGCATTGAAGTCAG
TGCTTCCGGAACGGCCAGGAAGAGAAGGCTGGGGTGGTGTCCA
CGGGCCTGATCCAGAATGGAGACTGGACCTTCCAGACCCTGGT
GATGCTAGAAACATTTCTCGGAGTGGAGAGGTTTACACCTGC
CAAGTGGAGCACCCAAGCGTAACGAGCCCTCTCACAGTGAAT
GGAGTGCACGGTCTGAATCTGCACAGAGCAAGATGCTGAGTGG
AGTCGGGGGCTTTGTGCTGGGCCTGCTCTTCCTTGGGGCCGGG
CTGTTTCTACTTTCAGGAATCAGAAAGGACACTCTGGACTTC
AGCCAACAGGATTCCTGAGC;

(ii) GGGGACACCCGACCACGTTTCTTGGAGCAGGTTAAACATGAGT
GTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGACAG
ATACTTCTATCACCAAGAGGAGTACGTGCGCTTCGACAGCGAC
GTGGGGGAGTACCGGGCCGTGACGGAGCTGGGGCGGCCTGATG
CCGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCG

GGCCGCGGTGGACACCTACTGCAGACACAACCTACGGGGTTGGT
GAGAGCTTCACAGTGCAGCGGCGAGTCTATCCTGAGGTGACTG
TGTATCCTGCAAAGACCCAGCCCCCTGCAGCACCACAACCTCCT
GGTCTGCTCTGTGAATGGTTTCTATCCAGGCAGCATTGAAGTC
AGGTGGTTCCGGAACGGCCAGGAAGAGAAGACTGGGGTGGTGT
CCACAGGCCTGATCCAGAATGGAGACTGGACCTTCCAGACCCT
GGTGATGCTGGAAACAGTTCCTCGGAGTGGAGAGGTTTACACC
TCCCAAGTGGAGCACCCAAGCCTGACGAGCCCTCTCACAGTGG
AATGGAGAGCACGGTCTGAATCTGCACAGAGCAAGATGCTGAG
TGGAGTCGGGGGCTTCGTGCTGGGCCTGCTCTTCCTTGGGGCC
GGGCTGTTCATCTACTTCAGGAATCAGAAAGGACACTCTGGAC
TTCAGCCAACAGGATTCCTGAGC;

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(iii) a DNA sequence which is fully complementary
to the DNA sequence of (i) or (ii); and

(iv) a DNA sequence which differs from the DNA
sequence of (i) or (ii) in codon sequence
due to the degeneracy of the genetic code;
and

(d) detecting hybridization between said size-
fractionated DNA and said second DNA.

57. An HLA-DR typing process comprising the steps
of:

(a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence encoding a majority of the region defined by amino acids:

- (i) 8-14,
- (ii) 26-32,
- (iii) 39-45, or
- (iv) 72-78

of the polypeptide coded for by DNA insert DR- β -A, DR- β -B, DR- β -C or allelic variants thereof; and

(b) detecting the hybridization between said DNA in said sample and said DNA sequence.

172 58. An HLA-DR typing process comprising the steps of:

(a) restricting a first DNA isolated from an individual to be typed with at least one restriction endonuclease;

(b) size-fractionating said restricted DNA;

(c) hybridizing the size-fractionated DNA to a second DNA, said second DNA being characterized by a nucleotide sequence encoding a majority of the region defined by amino acids:

- (i) 8-14,
- (ii) 26-32,
- (iii) 39-45, or
- (iv) 72-78

of the polypeptide coded for by DNA insert DR- β -A, DR- β -B, DR- β -C or allelic variants thereof; and

(d) detecting areas of hybridization between said size-fractionated DNA and said second DNA.

59. The HLA-DR typing process according to claim 57 or 58, wherein said second DNA is characterized by a nucleotide sequence selected from the group consisting of:

TGGAGCTGCTTAAGTCTGA, TCCTGGAGAGACACTTCCA,
GGGGCCAGGTGGACAATTA, TGGAGCAGGTAAACATGA, TCCTGGACAGATACTTCTA
and GGGCCGCGGTGGACACCTA.

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60. The HLA-DR typing process according to any one of claims 51, 53, 55 or 57, further comprising the step of comparing said hybridization to hybridization between DNA of known HLA-DR type and said DNA sequence.

61. The HLA-DR typing process according to any one of claims 52, 54, 56 or 58, further comprising the step of comparing said hybridization to hybridization between DNA of known HLA-DR type and said second DNA.

62. The HLA-DR typing process according to any one of claims 51, 53, 55 or 57 wherein prior to the step of detecting said areas of hybridization, the process further comprises the step of hybridizing said DNA in said sample to a

hybridization control, said hybridization control being a DNA having the nucleotide sequence: GCTTCGACAGCGACGTGGG.

63. The HLA-DR typing process according to any one of claims 52, 54, 56 or 58, wherein prior to the step of detecting said areas of hybridization, the process further comprises the step of hybridizing said size-fractionated DNA to a hybridization control, said hybridization control being a DNA having the nucleotide sequence: GCTTCGACAGCGACGTGGG.

P2 64. The HLA-DR typing process according to any one of claims 51, 53, 55, 57 or 70, wherein said DNA sequence is a labeled DNA sequence and its label is used for detecting hybridization between said DNA in said sample and said DNA sequence.

65. The HLA-DR typing process according to any one of claims 52, 54, 56, 58 or 71, wherein said second DNA is a labeled DNA and its label is used for detecting hybridization between said size-fractionated DNA and said second DNA.

66. An HLA-DR typing kit comprising a DNA sequence selected from the group consisting of:

- (i) the DNA sequence of DNA insert DR- β -A, DR- β -B or DR- β -C;
- (ii) the expressed portion of the DNA sequence of DNA insert DR- β -A, DR- β -B or DR- β -C;

- (iii) a DNA sequence that, upon expression, codes for a portion of a polypeptide encoded by any one of the foregoing DNA sequences, said portion comprising a region of mismatch between any two of the foregoing DNA sequences;
- (iv) a DNA sequence that hybridizes to any one of the foregoing sequences; and
- (v) a DNA sequence which differs from any one of the foregoing DNA sequences in codon sequence due to the degeneracy of the genetic code!

102 67. An HLA-DR typing kit comprising a DNA sequence which hybridizes to an HLA-DR- β chain locus, said DNA sequence being capable of hybridizing to a polymorphic region of said locus to allow determination of one or more HLA alleles for use in HLA-DR- β typing, said polymorphic region being encoded by a DNA sequence selected from the group consisting of:

- (i) a DNA sequence encoding amino acids 8-14, 26-32 or 72-78 of said locus;
- (ii) a portion of any one of the foregoing DNA sequences which is capable of hybridizing to said polymorphic region;
- (iii) a DNA sequence which differs from any one of the foregoing DNA sequences in codon

sequence due to the degeneracy of the genetic code; and

- (iv) a DNA sequence which is fully complementary to any one of the foregoing DNA sequences.

68. The HLA-DR typing kit according to claim 66 or 67, wherein said DNA sequence is labeled.

69. The HLA-DR typing kit according to claim 66 or 67, further comprising a 19-mer hybridization control being a DNA having the nucleotide sequence: GCTTCGACAGCGACGTGGG.

70. An HLA-DR typing process comprising the steps of:

102 (a) hybridizing DNA in a sample to be typed to a DNA sequence, said DNA sequence being capable of hybridizing to a conserved region of an HLA- β chain locus to allow determination of an HLA- β chain for use in HLA-DR- β typing, said conserved region being encoded by DNA selected from the group consisting of:

- (i) a DNA sequence encoding amino acids 39-45 of said locus;
- (ii) a DNA sequence which is fully complementary to any one of the DNA sequences of (i); and
- (iii) a DNA sequence which differs from any one of the DNA sequences of (i) in

codon sequence due to the degeneracy
of the genetic code; and

(b) detecting areas of hybridization between said
DNA in said sample and said DNA sequence.

71. An HLA-DR typing process comprising the steps
of:

(a) restricting a first DNA isolated from an
individual to be typed with at least one restriction
endonuclease;

(b) size-fractionating said restricted DNA;

172 (c) hybridizing DNA in a sample to be typed to a DNA
sequence, said DNA sequence being capable of hybridizing to a
conserved region of an HLA- β chain locus to allow determination
of an HLA- β chain for use in HLA-DR- β typing, said conserved
region being encoded by DNA selected from the group consisting
of:

- (i) a DNA sequence encoding amino acids
39-45 of said locus;
- (ii) a DNA sequence which is fully
complementary to any one of the DNA
sequences of (i); and
- (iii) a DNA sequence which differs from any
one of the DNA sequences of (i) in
codon sequence due to the degeneracy
of the genetic code; and

(d) detecting areas of hybridization between said size-fractionated DNA and said second DNA.

72. An HLA-DR typing kit comprising a DNA sequence which hybridizes to an HLA- β chain locus, said DNA sequence being capable of hybridizing to a conserved region of said locus to allow determination of a DR- β chain for use in HLA-DR- β typing, said conserved region being encoded by a DNA sequence selected from the group consisting of:

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- (i) a DNA sequence encoding amino acids 39-45 of said locus;
 - (ii) a portion of any one of the foregoing DNA sequences which is capable of hybridizing to said conserved region;
 - (iii) a DNA sequence which differs from any one of the foregoing DNA sequences in codon sequence due to the degeneracy of the genetic code; and
 - (iv) a DNA sequence which is fully complementary to any one of the foregoing DNA sequences.

REMARKS

Applicants have amended the specification to amend the status of this application to that of a divisional of parent application United States Serial No. 07/902,999 (now United States patent 5,503,976). In addition, applicants have